In the Claims:

Please amend claims 46 and 47 as indicated below.*

46. (Amended) A method for producing a human IgM comprising a nonchimeric variable region, wherein said immunoglobulin is specific for a desired antigen, wherein said method comprises the steps of:

(a) administering said antigen or an immunogenic portion thereof to a transgenic mouse under conditions to stimulate an immune response, whereby said animal produces B cells that produce said immunoglobulin specific for said antigen,

wherein the genome of said transgenic mouse is characterized by inactivated endogenous immunoglobulin heavy chain loci in which all of the J segment genes are deleted to prevent rearrangement of the loci and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, and by inactivated endogenous immunoglobulin light chain loci in which genes are deleted to prevent rearrangement of the loci and to prevent formation of a transcript of a rearranged immunoglobulin light chain locus,

and wherein said genome of said transgenic mouse further comprises a DNA fragment of a human immunoglobulin heavy chain locus, the fragment being a SpeI-SpeI fragment commencing from the VH6 gene and continuing through the human D segment genes, human J segment genes and human constant region genes and into the Cδ gene of that locus, wherein said SpeI-SpeI fragment does not include a gamma constant region, and further comprises a fragment of human chromosome 2, said fragment comprising Vκ, Jκ and Cκ gene segments of a human immunoglobulin kappa light chain locus, and

(b) recovering said immunoglobulin, provided that if said immunoglobulin comprises a human constant region, said human constant region is a human mu constant region or a human kappa constant region, or both.

47. (Amended) A method for producing an antigen binding fragment

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* An Appendix of Amended Claims is attached hereto, highlighting all the claim amendments with brackets (deletions) and underlines (insertions).

of a human IgM, said fragment comprising a nonchimeric variable region, wherein said fragment is specific for a desired antigen, wherein said method comprises the steps of:

(a) administering said antigen or an immunogenic portion thereof to a transgenic mouse under conditions to stimulate an immune response, whereby said animal produces B cells that produce said immunoglobulin specific for said antigen,

wherein the genome of said transgenic mouse is characterized by inactivated endogenous immunoglobulin heavy chain loci in which all of the J segment genes are deleted to prevent rearrangement of the loci and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, by inactivated endogenous immunoglobulin light chain loci in which one or more genes are deleted to prevent rearrangement of the loci and to prevent formation of a transcript of a rearranged immunoglobulin light chain locus,

and wherein said genome of said transgenic mouse further comprises a DNA fragment of a human immunoglobulin heavy chain locus, the fragment being a SpeI-SpeI fragment commencing from the VH6 gene and continuing through the human D segment genes, human J segment genes and human constant region genes and into the Cδ gene of that locus, wherein said SpeI-SpeI fragment does not include a gamma constant region, and further comprises a fragment of human chromosome 2, said fragment comprising Vκ, Jκ and Cκ gene segments of a human immunoglobulin kappa light chain locus,

(b) recovering said immunoglobulin specific for said antigen, and

(c) producing an antigen-binding fragment from said immunoglobulin recovered in step (b).

REMARKS

Claims 2, 3, 46 and 47 are pending. Of these, claims 46 and 47 have been amended to recite "human IgM" and "nonchimeric variable region" in the preamble. Support for these amendments appears throughout the specification, e.g., at pp. 21-38.

The Examiner points out that the incorporation of WO 94/02602 in its entirety at pages 39-141 of the specification was improperly made in applicants' June 20, 2001 *Amendment and Response*. Per the Examiner's request, applicants herein expressly